

Amendment

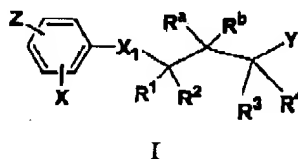
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USSN 09/848,697  
QA211NPAmendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1. (Currently Amended) A compound of the formula



wherein  $X_1$  is O,  $S(O)_n$ ,  $-N(R^5)-$ ,  $CO-N(R^6)-$ , or  $-CH_2-$ , with the proviso that when  $X_1$  is  $-CH_2-$ ,  $R^1$  and  $R^2$  are only halogen;

$n$  is 0, 1 or 2;

$R^a$  and  $R^b$  when taken together form an oxo ( $=O$ ) group, or  $R^a$  and  $R^b$  are each independently hydrogen, OH,  $OCOR^9$ ,  $NH_2$ ,  $N_3$ ,  $NHCOOR^9$ ,  $NHCOCOR^9$ ,  $NHSO_2R^9$  or F;

$X$  is H,  $CF_3$ ,  $OCF_3$ , halogen,  $C_1-C_7$  alkyl,  $C_2-C_7$  alkenyl,  $C_2-C_7$  alkynyl or  $C_3-C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl or cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , heterocyclic,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ , or aryl or heteroaryl, said aryl or heteroaryl being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^9$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocyclic;

$R^1$  and  $R^2$  are each independently H, halogen,  $OR^9$ ,  $C_1-C_7$  alkyl,  $C_2-C_7$  alkynyl,

O.K. to enter Sk. 10/19/04

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C<sub>2</sub>-C<sub>7</sub> alkaryl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH, S(O)<sub>n</sub>R<sup>9</sup>, NR<sup>6</sup>R<sup>7</sup>, NH(CO)NR<sup>6</sup>R<sup>7</sup>, NH(CO)OR<sup>9</sup>, OC(O)OR<sup>9</sup>, or aryl or heteroaryl, said aryl and heteroaryl being optionally substituted with one or two groups independently selected from NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>, COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, OCOR<sup>9</sup>, PO<sub>3</sub>R<sup>8</sup>, and C(O)NR<sup>6</sup>R<sup>7</sup> and heterocyclic;

R<sup>3</sup>, R<sup>4</sup> and Y are each independently H, halogen, OR<sup>10</sup>, S(O)<sub>n</sub>R<sup>10</sup>, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH, S(O)<sub>n</sub>R<sup>9</sup>, NR<sup>6</sup>R<sup>7</sup>, NH(CO)NR<sup>6</sup>R<sup>7</sup>, NH(CO)OR<sup>9</sup>, OC(O)OR<sup>9</sup>, or aryl or heteroaryl, said aryl and heteroaryl being optionally substituted by one or two groups independently selected from NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>, COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, OCOR<sup>8</sup>, PO<sub>3</sub>R<sup>8</sup>, and C(O)NR<sup>6</sup>R<sup>7</sup> and heterocyclic, with the proviso that not all of R<sup>3</sup>, R<sup>4</sup> and Y may be the same halogen;

R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are each independently H, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, OR<sup>8</sup>, NR<sup>8</sup>R<sup>9</sup>, SO<sub>3</sub>R<sup>8</sup>, PO<sub>3</sub>R<sup>8</sup>, halogen, or aryl or heteroaryl, said aryl or heteroaryl being optionally substituted by one or two groups independently selected from COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, and PO<sub>3</sub>R<sup>8</sup> and heterocyclic;

R<sup>8</sup> is H, C<sub>1</sub>-C<sub>7</sub> saturated straight chain alkyl or cycloalkyl;

R<sup>9</sup> is C<sub>1</sub>-C<sub>7</sub> saturated straight chain alkyl or cycloalkyl;

R<sup>10</sup> is C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally substituted by

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COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH, S(O)<sub>n</sub>R<sup>9</sup>,  
NR<sup>6</sup>R<sup>7</sup>, NH(CO)NR<sup>6</sup>R<sup>7</sup>, NH(CO)OR<sup>9</sup>, or aryl or heteroaryl, said aryl or heteroaryl  
being optionally substituted by one or two groups independently selected from  
NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>, COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, OCOR<sup>8</sup>, PO<sub>3</sub>R<sup>8</sup>, and C(O)NR<sup>6</sup>R<sup>7</sup> and heterocyclic;

Z is OR<sup>11</sup>, S(O)<sub>n</sub>R<sup>11</sup>, NR<sup>11</sup>R<sup>12</sup> or CHR<sup>11</sup>R<sup>12</sup>;

R<sup>11</sup> is C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl,  
alkenyl, alkynyl or cycloalkyl group being substituted by NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>n</sub>R<sup>13</sup>, or  
OR<sup>13</sup>;

R<sup>12</sup> is hydrogen, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
said alkyl, alkenyl, alkynyl or cycloalkyl group being optionally substituted by  
NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>n</sub>R<sup>13</sup>, or OR<sup>13</sup>;

R<sup>13</sup> is ~~SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>~~, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-C<sub>7</sub>  
cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being substituted by  
one to three groups independently selected from COOR<sup>8</sup>, OR<sup>8</sup>, ~~SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>~~,  
OR<sup>15</sup>, aryl, and biaryl and heteroaryl, said aryl[[.]] and biaryl and heteroaryl being  
optionally substituted with one to three groups independently selected from halogen,  
CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, and CN;

R<sup>14</sup> is H, ~~SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>~~, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-  
C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally  
substituted by one to three groups independently selected from COOR<sup>8</sup>, OR<sup>8</sup>, Si  
~~R<sup>15</sup>R<sup>16</sup>R<sup>17</sup>~~, OR<sup>15</sup>, aryl, and biaryl and heteroaryl, said aryl[[.]] and biaryl and  
heteroaryl being optionally substituted with one to three groups independently  
selected from halogen, CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, and CN; and ~~or~~

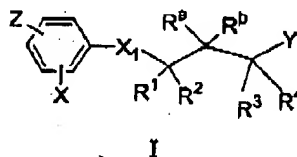
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~~R<sup>13</sup> and R<sup>14</sup> when taken together with the nitrogen atom to which they are attached may form a 5-7 membered heterocyclic ring with one or more heteroatoms selected from O, N and S; said ring being optionally substituted by OR<sup>8</sup>, COOR<sup>8</sup>, or C(O)NR<sup>6</sup>R<sup>6</sup>; and~~

~~R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup> are each independently is C<sub>1</sub>-C<sub>7</sub> alkyl, aryl, benzyl, benzhydryl, biaryl, heteroaryl, or (C<sub>1</sub>-C<sub>6</sub>) alkyl-aryl or (C<sub>1</sub>-C<sub>6</sub>) alkyl-heteroaryl, said aryl, benzyl, benzhydryl, and biaryl being optionally substituted by halogen, CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, CN, or C<sub>1</sub>-C<sub>7</sub> alkyl.~~

Claim 2. (Currently Amended) A compound of the formula



or a pharmaceutically acceptable salt thereof wherein

X<sub>1</sub> is O, S(O)<sub>n</sub>,  $\text{---}\overset{\text{R}^5}{\text{N}}\text{---}$ ,  $\text{CO---}\overset{\text{R}^6}{\text{N}}\text{---}$  or  $\text{---CH}_2\text{---}$ , with the proviso that when X<sub>1</sub> is  $\text{---CH}_2\text{---}$ , R<sup>1</sup> and R<sup>2</sup> are only halogen;

n is 0, 1 or 2;

R<sup>a</sup> and R<sup>b</sup> when taken together form an oxo (=O) group, or R<sup>a</sup> and R<sup>b</sup> are each independently hydrogen, OH, OCOR<sup>9</sup>, NH<sub>2</sub>, N<sub>3</sub>, NHCOOR<sup>9</sup>, NHCOCOR<sup>9</sup>, NHSO<sub>2</sub>R<sup>9</sup> or F;

X is H, CF<sub>3</sub>, OCF<sub>3</sub>, halogen, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl or cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH,

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$S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ , or aryl or heteroaryl, said aryl or heteroaryl being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^9$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocycloalkyl;

$R^1$  and  $R^2$  are each independently H, halogen,  $OR^9$ ,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkynyl,  $C_2$ - $C_7$  alkenyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , heterocycloalkyl,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ ,  $OC(O)OR^9$ , or aryl or heteroaryl, said aryl and heteroaryl being optionally substituted with one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^9$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocycloalkyl;

$R^3$ ,  $R^4$  and Y are each independently H,  $OR^{10}$ ,  $S(O)_nR^{10}$ ,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkynyl,  $C_2$ - $C_7$  alkenyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , heterocycloalkyl,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ ,  $OC(O)OR^9$ , or aryl or heteroaryl, said aryl and heteroaryl being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^8$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocycloalkyl;

$R^5$ ,  $R^6$  and  $R^7$  are each independently H,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkenyl,  $C_2$ - $C_7$  alkynyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $OR^8$ ,  $NR^8R^9$ ,  $SO_3R^8$ ,  $PO_3R^8$ , halogen, or aryl or heteroaryl, said aryl and heteroaryl being optionally substituted by one or two groups independently selected from  $COOR^8$ ,  $SO_3R^8$ , and  $PO_3R^8$  and heterocycloalkyl;

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$R^8$  is H, C<sub>1</sub>-C<sub>7</sub> saturated straight chain alkyl or cycloalkyl, CF<sub>3</sub> or CH<sub>2</sub>CF<sub>3</sub>;

$R^9$  is C<sub>1</sub>-C<sub>7</sub> saturated straight chain alkyl or cycloalkyl;

$R^{10}$  is C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH, S(O)<sub>n</sub>R<sup>9</sup>, NR<sup>6</sup>R<sup>7</sup>, NH(CO)NR<sup>6</sup>R<sup>7</sup>, NH(CO)OR<sup>9</sup>, or aryl or heteroaryl, said aryl or heteroaryl being optionally substituted by one or two groups independently selected from NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>, COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, OCOR<sup>8</sup>, PO<sub>3</sub>R<sup>8</sup>, and C(O)NR<sup>6</sup>R<sup>7</sup> and heterocyclic;

Z is OR<sup>11</sup>, S(O)<sub>n</sub>R<sup>11</sup>, NR<sup>11</sup>R<sup>12</sup> or CHR<sup>11</sup>R<sup>12</sup>;

$R^{11}$  is C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl or cycloalkyl group being substituted by NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>n</sub>R<sup>13</sup>, or OR<sup>13</sup>;

$R^{12}$  is hydrogen, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl or cycloalkyl group being optionally substituted by NR<sup>13</sup>R<sup>14</sup>, S(O)<sub>n</sub>R<sup>13</sup> or OR<sup>13</sup>;

$R^{13}$  is SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being substituted by one to three groups independently selected from COOR<sup>8</sup>, OR<sup>8</sup>, SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>, OR<sup>15</sup>, aryl, and biaryl and heteroaryl, said aryl[[.]] and biaryl and heteroaryl being optionally substituted with one to three groups independently selected from halogen, CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, and CN;

$R^{14}$  is H, SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>, C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-

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C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally substituted by one to three groups independently selected from COOR<sup>8</sup>, OR<sup>8</sup>, SiR<sup>15</sup>R<sup>16</sup>R<sup>17</sup>, OR<sup>15</sup>, aryl, and biaryl and heteroaryl, said aryl[,] and biaryl and heteroaryl being optionally substituted with one to three groups independently selected from halogen, CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, and CN; and or

~~R<sup>13</sup> and R<sup>14</sup> when taken together with the nitrogen atom to which they are attached may form a 5-7 membered heterocyclic ring with one or more heteroatoms selected from O, N and S; said ring being optionally substituted by OR<sup>8</sup>, COOR<sup>8</sup>, or C(O)NR<sup>5</sup>R<sup>6</sup>; and~~

R<sup>15</sup>, ~~R<sup>16</sup>, R<sup>17</sup>~~ are each independently is C<sub>1</sub>-C<sub>7</sub> alkyl, aryl, benzyl, benzhydryl, biaryl, heteroaryl, or (C<sub>1</sub>-C<sub>6</sub>) alkyl-aryl or (C<sub>1</sub>-C<sub>6</sub>) alkyl-heteroaryl, said aryl, benzyl, benzhydryl, and biaryl being optionally substituted by halogen, CF<sub>3</sub>, OR<sup>8</sup>, COOR<sup>8</sup>, NO<sub>2</sub>, CN, or C<sub>1</sub>-C<sub>7</sub> alkyl.

Claim 3. (Currently Amended) A compound of claim 2 wherein X<sub>1</sub> is O or S(O)<sub>n</sub> and Y is OR<sup>10</sup> in which R<sup>10</sup> is C<sub>1</sub>-C<sub>7</sub> alkyl, C<sub>2</sub>-C<sub>7</sub> alkenyl, C<sub>2</sub>-C<sub>7</sub> alkynyl, aryl or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally substituted by COOR<sup>8</sup>, CN, C(O)NR<sup>6</sup>R<sup>7</sup>, PO<sub>3</sub>R<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, heterocyclic, OR<sup>8</sup>, SH, S(O)<sub>n</sub>R<sup>9</sup>, NR<sup>6</sup>R<sup>7</sup>, NH(CO)NR<sup>6</sup>R<sup>7</sup>, NH(CO)OR<sup>9</sup>, or aryl or heteroaryl, said aryl or heteroaryl being optionally substituted by one or two groups independently selected from NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>, COOR<sup>8</sup>, SO<sub>3</sub>R<sup>8</sup>, OCOR<sup>9</sup>, PO<sub>3</sub>R<sup>8</sup>, and C(O)NR<sup>6</sup>R<sup>7</sup> or heterocyclic, said R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> substituents being defined as in claim 2.

Claim 4. (Original) A compound of claim 3 in which R<sup>a</sup> and R<sup>b</sup> taken together represent an oxo (=O) group, or R<sup>a</sup> and R<sup>b</sup> are each independently hydrogen or OH.

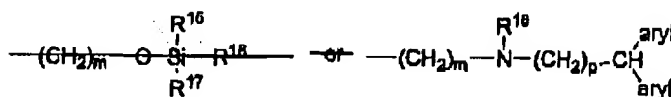
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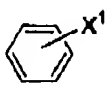
Claims 5-6. (Canceled).

Claim 7. (Currently Amended) A compound of claim 3 in which

Z is



in which m and p each independently represent an integer of one to six,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$  are each independently  $C_1$ - $C_7$  alkyl or phenyl,  $R^{18}$  is  $C_1$ - $C_7$  alkyl and aryl

represents  in which  $X^1$  is halogen.

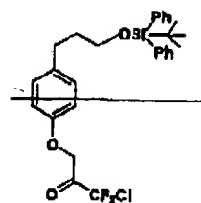
Claim 8. (Canceled).

Claim 9. (Original) A pharmaceutical composition for the inhibition of cytosolic phospholipase  $A_2$  comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

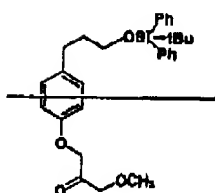
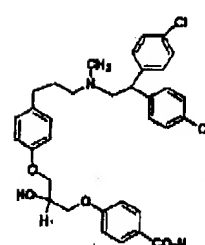
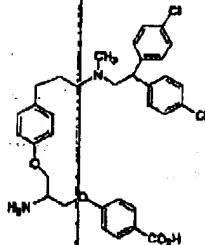
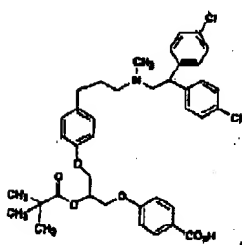
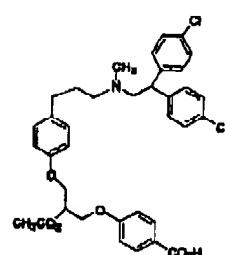
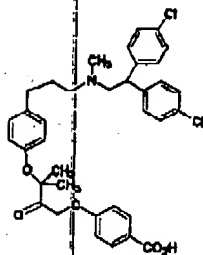
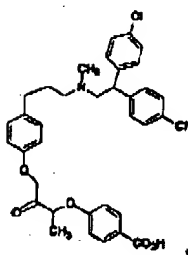
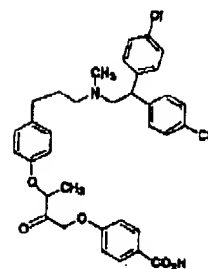
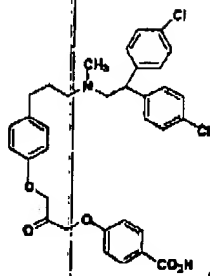
Claim 10. (Withdrawn) A method of inhibiting cytosolic phospholipase  $A_2$  in a mammal in need thereof, comprising administering to said mammal a therapeutically effective amount of a compound of claim 1.

Claim 11. (Currently Amended) A compound selected from

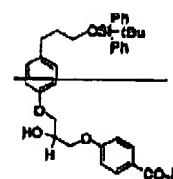
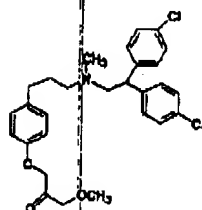
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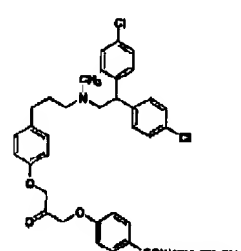
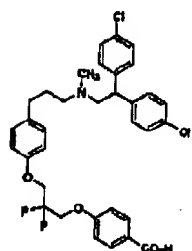
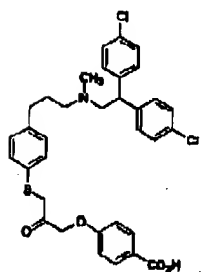
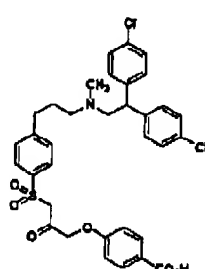
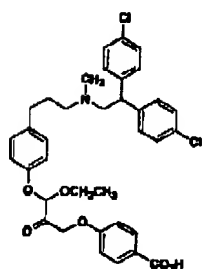
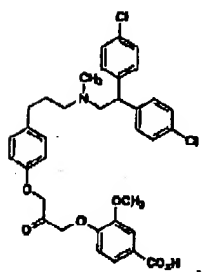
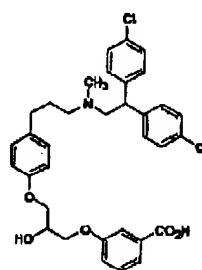
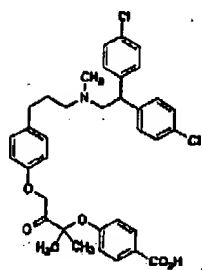
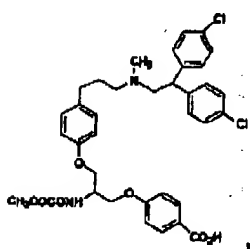
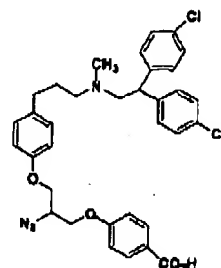
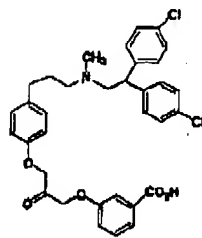
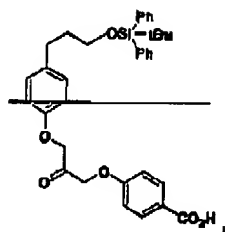


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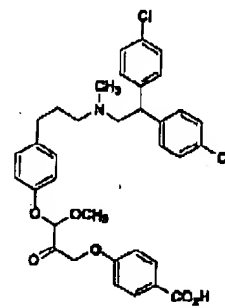
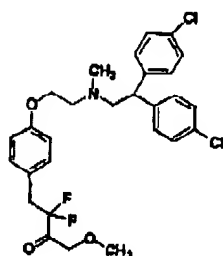
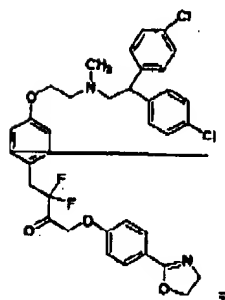
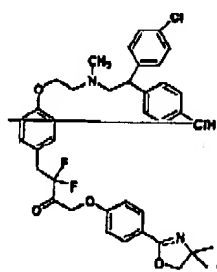
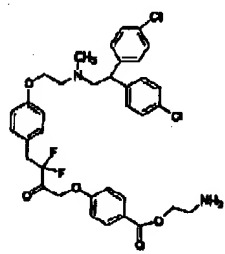
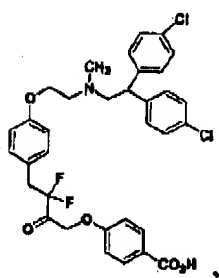
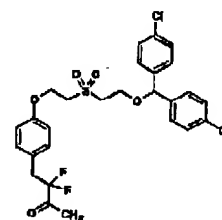
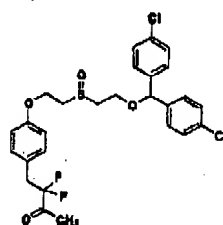
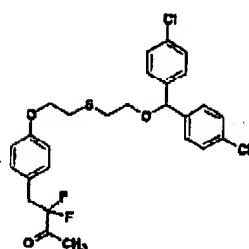
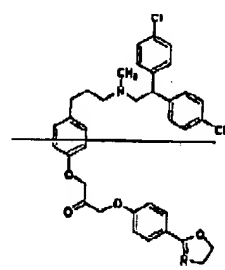
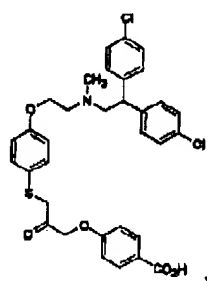
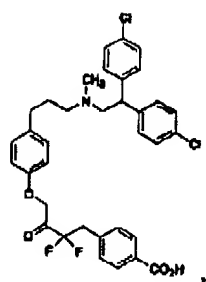


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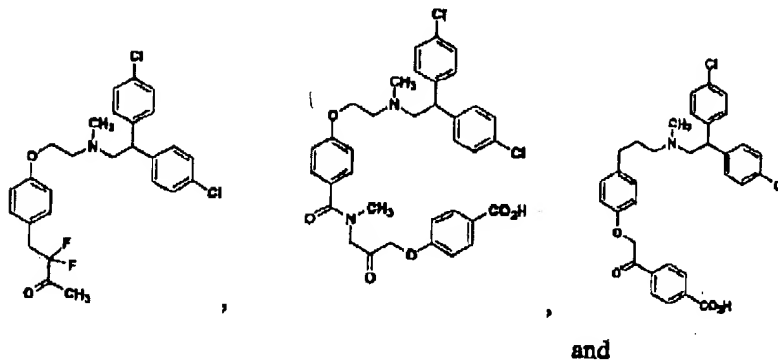
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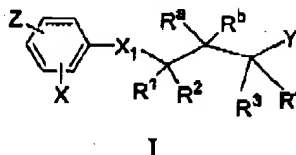
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or a pharmaceutically acceptable salt thereof.

Claim 12. (Currently Amended) A compound of the formula



or a pharmaceutically acceptable salt thereof wherein

$X_1$  is O,  $S(O)_n$ ,  $CO-N^{R^6}-$ , or  $-CH_2-$ , with the proviso that when  $X_1$  is  $-CH_2-$ ,  $R^1$  and  $R^2$  are only halogen;

$n$  is 0, 1 or 2;

$R^a$  and  $R^b$  when taken together form an oxo ( $=O$ ) group, or  $R^a$  and  $R^b$  are each independently hydrogen, OH,  $OCOR^9$ ,  $NH_2$ ,  $N_3$ ,  $NHCOCOR^9$ , or F;

$X$  is H;

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$R^1$  and  $R^2$  are each independently H, halogen,  $OR^9$ , or  $C_1-C_7$  alkyl;

$R^3$ ,  $R^4$  and Y are each independently H, halogen,  $OR^{10}$ , or  $C_1-C_7$  alkyl, said alkyl being optionally substituted by aryl, said aryl being optionally substituted by one or two  $COOR^8$  groups, with the proviso that not all of  $R^3$ ,  $R^4$  and Y may be the same halogen;

$R^5$ ,  $R^6$ , and  $R^7$  are each independently hydrogen or  $C_1-C_7$  alkyl, said alkyl being optionally substituted by  $OR^8$ ;

$R^8$  is H or  $C_1-C_7$  saturated straight chain alkyl;

$R^9$  is  $C_1-C_7$  saturated straight chain alkyl;

$R^{10}$  is  $C_1-C_7$  alkyl or aryl, said alkyl or aryl group being optionally substituted by  $COOR^8$ ,  $C(O)NR^6R^7$ , heterocyclic, or  $OR^8$ ;

Z is  $OR^{11}$  or  $CHR^{11}R^{12}$ ;

$R^{11}$  is  $C_1-C_7$  alkyl substituted by  $NR^{13}R^{14}$ ,  $S(O)_nR^{13}$ , or  $OR^{13}$ ;

$R^{12}$  is hydrogen;

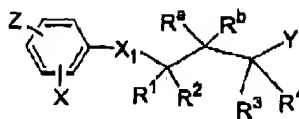
$R^{13}$  is  ~~$SiR^{15}R^{16}R^{17}$~~  or  $C_1-C_7$  alkyl, said alkyl substituted by one to three groups independently selected from  $OR^{15}$  and aryl, said aryl substituted with one halogen;

$R^{14}$  is  $C_1-C_7$  alkyl; and

$R^{15}$ ,  $R^{16}$ , and  $R^{17}$  ~~are each independently~~ is  $C_1-C_7$  alkyl, aryl, or benzhydryl, said aryl and benzhydryl being optionally substituted by halogen.

Claim 13. (Currently Amended) A compound of the formula

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or a pharmaceutically acceptable salt thereof wherein

$X_1$  is O,  $S(O)_n$ , or  $-CH_2-$ , with the proviso that when  $X_1$  is  $-CH_2-$ ,  $R^1$  and  $R^2$  are only halogen;

$n$  is 0, 1 or 2;

$R^a$  and  $R^b$  are each independently hydrogen, OH,  $OCOR^9$ ,  $NH_2$ ,  $N_3$ ,  $NHCOOR^9$ ,  $NHCOCOR^9$ , or F;

$X$  is H,  $CF_3$ ,  $OCF_3$ , halogen,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkenyl,  $C_2$ - $C_7$  alkynyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl or cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , heterocyclic,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ , or aryl or heteroaryl; said aryl or heteroaryl being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^9$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocyclic;

$R^1$  and  $R^2$  are each independently H, halogen,  $OR^9$ ,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkynyl,  $C_2$ - $C_7$  alkenyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , heterocyclic,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ ,  $OC(O)OR^9$ , or aryl or heteroaryl; said aryl and heteroaryl being optionally substituted with one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^9$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocyclic;

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$R^3$  and  $R^4$  are each independently H, halogen,  $OR^{10}$ ,  $S(O)_nR^{10}$ ,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkenyl,  $C_2$ - $C_7$  alkynyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , ~~heterocyclic~~,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ ,  $OC(O)OR^9$ , ~~or aryl or heteroaryl~~, said aryl and heteroaryl being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^8$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  and heterocyclic, ~~with the proviso that not all of  $R^3$ ,  $R^4$  and Y may be the same halogen.~~

Y is  $OR^{10}$  or  $S(O)_nR^{10}$ ;

$R^5$ ,  $R^6$  and  $R^7$  are each independently H,  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkenyl,  $C_2$ - $C_7$  alkynyl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl and cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $OR^8$ ,  $NR^8R^9$ ,  $SO_3R^8$ ,  $PO_3R^8$ , halogen, ~~or aryl or heteroaryl~~, said aryl ~~or heteroaryl~~ being optionally substituted by one or two groups independently selected from  $COOR^8$ ,  $SO_3R^8$ , and  $PO_3R^8$  ~~and heterocyclic~~;

$R^8$  is H,  $C_1$ - $C_7$  saturated straight chain alkyl or cycloalkyl;

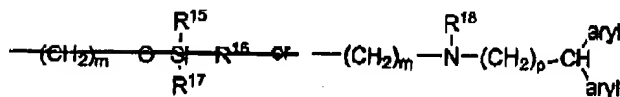
$R^9$  is  $C_1$ - $C_7$  saturated straight chain alkyl or cycloalkyl;

$R^{10}$  is  $C_1$ - $C_7$  alkyl,  $C_2$ - $C_7$  alkenyl,  $C_2$ - $C_7$  alkynyl, aryl or  $C_3$ - $C_7$  cycloalkyl, said alkyl, alkenyl, alkynyl, aryl or cycloalkyl group being optionally substituted by  $COOR^8$ , CN,  $C(O)NR^6R^7$ ,  $PO_3R^8$ ,  $SO_3R^8$ , ~~heterocyclic~~,  $OR^8$ , SH,  $S(O)_nR^9$ ,  $NR^6R^7$ ,  $NH(CO)NR^6R^7$ ,  $NH(CO)OR^9$ , ~~or aryl or heteroaryl~~, said aryl ~~or heteroaryl~~ being optionally substituted by one or two groups independently selected from  $NR^6R^7$ ,  $OR^8$ ,  $COOR^8$ ,  $SO_3R^8$ ,  $OCOR^8$ ,  $PO_3R^8$ , and  $C(O)NR^6R^7$  ~~or heterocyclic~~;  
and

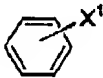
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Z is



in which m and p each independently represent an integer of one to six,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$  are each independently  $C_1$ - $C_7$  alkyl or phenyl,  $R^{18}$  is  $C_1$ - $C_7$  alkyl and aryl

represents  in which  $X^1$  is halogen.

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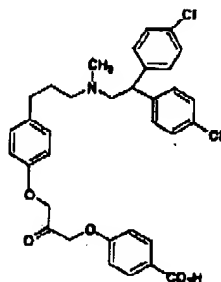
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QA211NPREMARKS/ARGUMENTS

Claims 1-4, 7, and 9-13 are pending in this application.

In the Office Action dated July 8, 2004, the Examiner rejected Claims 1-4, 9, 12, and 13 under 35 U.S.C. §102(b) as being unpatentable over JP 5-222006. Claim 7 was objected to as being dependent upon a rejected base claim.

Reconsideration and allowance of this application are respectfully requested in view of the above amendments and the remarks that follow.

Pursuant to the Examiner's request for an election of a single disclosed species on July 29, 2003, Applicants elected 3-[4-[3-[N-[2-Bis-(4-chlorophenyl)ethyl]-N-methylamino]propyl]phenoxy]-1-(4-carboxyphenoxy)-2-propanone which is Example 2 on page 51 of the specification.



3-[4-[3-[N-[2-Bis-(4-chlorophenyl)ethyl]-N-methylamino]propyl]phenoxy]-1-(4-carboxyphenoxy)-2-propanone

In the July 8, 2004 Office Action, the Examiner states that "Claim 11 will be allowed to the extent it reads on the elected subject matter. Compounds containing Silicon and heterocyclic subject matter should be deleted." Accordingly, Applicants have amended Claims 1, 2, 3, 7, 11, 12, and 13 to remove silicon and heterocyclic subject matter which reflects the scope of the generic concept of the elected subject matter. Applicants maintain the right to file divisional application(s) on non-elected subject matter.

Rejection of Claims 1-4, 9, 12, and 13 Under 35 U.S.C. §102(b)

The Examiner has rejected Claims 1-4, 9, 12, and 13 under 35 U.S.C. §102(b) as being unpatentable over JP 5-222006. JP'006 teaches compounds containing a

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heterocycle. It is Applicants' position that the amendments to Claims 1, 2, 3, 9, 12, and 13, which remove all heterocyclic subject matter, render the rejections moot. Therefore, it is respectfully requested that the rejections to Claims 1-4, 9, 12, and 13 be withdrawn.

**Objection of Claim 7 and Allowance of Claim 11**

Claim 7 has been objected to as being dependent upon a rejected base claim, but would be allowable to the extent that it reads on the elected subject matter, if rewritten in independent form including all of limitations of the base claim. The Examiner further states "Note applicants should delete Silicon containing subject matter." Applicants have amended Claim 7 to remove all silicon containing subject matter and respectfully request that the objection be withdrawn.

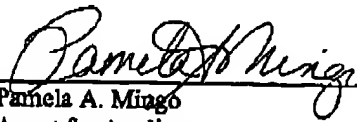
Claim 11 is allowed to the extent it reads on the elected subject matter. The Examiner further states "Compounds containing Silicon and heterocyclic subject matter should be deleted." Applicants have amended Claim 11 to remove all silicon and heterocyclic subject matter and respectfully request that the claim be allowed.

While Applicants submit that the claims are in condition for allowance and respectfully request the Examiner's reconsideration, a NOTICE OF APPEAL has nevertheless been filed. The Commissioner is hereby authorized to charge any additional fees under 37 CFR §1.17 which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

Bristol-Myers Squibb Company  
Patent Department  
P.O. Box 4000  
Princeton, NJ 08543-4000  
(203) 677-~~6000~~

9869  
Date: October 7, 2004

  
Pamela A. Mingo  
Agent for Applicants  
Reg. No. 48, 256